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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,520	LOIBNER ET AL.	
	Examiner	Art Unit	
	Brad Duffy	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 24, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *16,23,24,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-22 and 25-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/11/05, 8/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed May 24, 2007 is acknowledged and has been entered. Claims 8-11 and 23-24 have been amended. Claims 25-45 have been newly added.

2. The election with traverse filed May 24, 2007, is acknowledged and has been entered.

Applicant has elected the invention of Group IV, claim 17, drawn to methods for the intraoperative treatment of tumors comprising administering an antibody specific for Lewis Y during surgery. Additionally, claims 1-15 and 18-22 are linking claims that link inventions of Groups I-IX. Finally, newly added claims 26-43 are drawn to the elected invention of administering Lewis Y antibodies during surgery and newly added claim 25 is a linking claim that links inventions of Groups IV-VIII.

3. Claims 1-45 are pending in the application.

4. Claims 16, 23-24 and 44-45 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Notably, these claims have been withdrawn as they are directed to the invention of Group XI, drawn to methods of administering an antibody against a tumor-associated antigen before surgery. Applicant timely traversed the restriction (election) requirement in the reply filed on May 24, 2007.

5. Claims 1-15, 17-22 and 25-43 are under examination.

Response to Amendment

6. The amendment filed on May 24, 2007, is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see

68 Fed. Reg. 38611, Jun. 30, 2003). However, in order to advance prosecution, rather than mailing a Notice of Non-Compliant Amendment, Applicant is advised to correct the following deficiencies in replying to this Office action:

The amendment to the claims is considered non-compliant as it presents newly added claims with underlining. See 37 CFR § 1.121(c)(3) which states "Any claim added by amendment must be indicated with the status of "new " and presented in clean version, i.e., without any underlining."

Applicant is reminded: Only the corrected section(s) of the non-compliant amendment must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment must be re-submitted. 37 CFR § 1.121(h).

Election/Restrictions

7. Applicant's traversal of the restriction and election requirement set forth in the Office action mailed April 11, 2007, is acknowledged.

Applicant's arguments have been carefully considered but have not been found persuasive for the following reasons:

Applicant has argued, "no unity of invention objection was raised during the International Phase of this application [; so therefore,] Applicants submit that a similar finding should apply to this National Phase application" (see page 7, paragraph 4 of the response filed May 24, 2007). Applicant further argues on page 8 of this response: "An international application which complies with the PCT unity of invention requirements must then be accepted by all of the designated and elected offices including the USPTO, since Article 27 (1) of the Patent Cooperation Treaty does not permit any national law or national office to require compliance with different regulations relating to the contents of the international application. Thus, the U.S. application must be examined for unity of invention consistent with the Patent Cooperation Treaty, not just

by citation to PCT rules or apparent verbal assent to the standard, but rather in actual application and compliance of the standard. (see *Caterpillar Tractor Co. v. Commission of Patent and Trademarks*, 231 USPQ 590 (E.D.VA. 1986)".

In response, the Examiner is aware that this National Stage application must be examined for unity of invention consistent with the Patent Cooperation Treaty and it is noted that starting at page 5 of the restriction requirement mailed April 11, 2007, the Examiner determined that claim 1 lacks an inventive step over the prior art. Therefore, the Examiner determined in examining the inventions for unity of invention consistent with the Patent Cooperation Treaty that the inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

Finally, contrary to Applicant's argument that the Examiner is bound by the actions taken in the International Phase of this application, the Examiner is not bound by the actions that occurred in the international phase, as MPEP 1893.03(d) clearly states, "If the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted."

Additionally, at page 7 of the response, Applicant has argued, "the common inventive aspect which links the claims is not anticipated by the prior art cited by the Examiner".

In response, as set forth above, starting at page 5 of the restriction requirement mailed April 11, 2007, the Examiner determined that claim 1 lacks an inventive step over the prior art cited. Therefore, Applicant's arguments against the references individually, is not persuasive as the Applicant has not provided any reasoning or argument to establish that claim 1 defines an inventive step over the prior art cited.

Finally, Applicant has argued at page 8, 1st full paragraph, that "in making the restriction requirement, the Examiner also attempts to break up Applicants' generic claims, and thereby apparently refuse to examine Applicants' proper generic claims" and that "under 35 U.S.C. § 121, an Examiner can make a restriction requirement

between different groups of claims but cannot properly restrict an application by dividing up the subject matter of a single generic claim by making a restriction within that claim".

In response, as set forth at page 4 of the restriction requirement mailed April 11, 2006, the examiner has identified claims 1-15 and 18-22 as linking claims that link inventions of Groups I-IX[1]. As set forth in MPEP § 809, "The linking claims must be examined with, and thus are considered part of, the invention elected". Thus contrary to Applicant's arguments the Examiner is not limiting Applicants' generic claims as the linking claims are being examined along with the elected invention[2].

Then in response, to Applicant's arguments pertaining to making a restriction requirement within a single claim, MPEP § 1850 states the following:

> "Alternative forms of an invention may be claimed either in a plurality of independent claims, or in a single claim. In the latter case, the presence of the independent alternatives may not be immediately apparent. In either case, however, the same criteria should be applied in deciding whether there is unity of invention. Accordingly, lack of unity of invention may exist within a single claim. Where the claim contains distinct embodiments that are not linked by a single general inventive concept, the objection as to lack of unity of invention should be raised."

Notably, in order to clarify the reasoning why a method of administering an antibody specific for Lewis Y does not share unity of invention with, e.g., a method of administering an antibody specific for sialylated TN, it is noted that wherein each antibody comprises a unique structure that specifically binds a structurally and functionally distinct antigen, there is a presumption that none of these methods are related by the concept of "unity of invention".

M.P.E.P. § 803.02 states:

> [I]t is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

In this instance, although the different antibodies administered in claim 17 appear

[1] Claim 16 was inadvertently included as a linking claim, but as claim 16 is a product identified as the invention of Group X, it clearly does not link inventions of Groups I-IX

to share a common *prima facie* utility (i.e., the ability inhibit dissemination of tumor cells), none of the antibodies actually share a substantial structural feature essential to that utility because each different antibody comprises a structurally distinct antigen binding domain that results in each distinct antibody having different functional attributes. For example, in addition to each binding a different antigen, it has been recently noted that antibodies specific for the Lewis Y antigen are able to induce effective complement-dependent cytotoxicity against tumor cells derived from patients, while antibodies specific for sialylated TN were unable to induce effective complement-dependent cytotoxicity against tumor cells derived from patients[3].

Therefore, as set forth at page in the restriction requirement mailed April 11, 2007, it is maintained that the special technical feature of Group IV "is the inhibition of dissemination of tumor cells by a process comprising administering an antibody specific for LEWIS Y during surgery", which is different from the special technical features of Groups I-III and V-IX. Accordingly the restriction between the inventions of Groups I-XI is deemed proper.

Furthermore, Applicant has provided no evidence to establish why the remaining groups share unity of invention as required under PCT Rule 13 or why the requirement for restriction is improper.

Therefore, for these reasons and the reasons set forth in the Office action mailed April 11, 2007, these inventions do not share unity of invention as required under PCT Rule 13 and the restriction/election requirement is deemed proper and therefore made FINAL.

Priority

8. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

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[2] It is noted that claims 1-15 and 18-22 were inadvertently included in Group VIII, but as these are linking claims, Group VIII should clearly recite only Claim 17

Information Disclosure Statement

9. The patent documents cited in the information disclosure statements filed on February 11, 2005, and August 22, 2005, have been considered. Since document WO 00/69460 is listed on both IDSs, it was crossed out on the second IDS filed August 22, 2005.

Additionally, the non-patent literature publications listed of the information disclosure statements filed February 11, 2005, and August 22, 2005 were not considered as these citations fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Notably, in the information disclosure statement filed February 11, 2005 applicant submits that copies of these references should be forwarded from the International Search Authority. However, copies of these references were not in the file and the burden is on Applicant to supply such copies as their receipt was not indicated on Form PCT/DO/EO/903. See MPEP § 1893.03(g), which states the following:

> When all the requirements for a national stage application have been completed, applicant is notified (Form PCT/DO/EO/903) of the acceptance of the application under 35 U.S.C. 371, including an itemized list of the items received. The itemized list includes an indication of whether a copy of the international search report and copies of the references cited therein are present in the national stage file. The examiner will consider the documents cited in the international search report, without any further action by applicant under 37 CFR 1.97 and 1.98, when both the international search report and copies of the documents are indicated to be present in the national stage file. The examiner will note the consideration in the first Office action. There is no requirement that the examiners list the documents on a PTO-892 form. See form paragraphs 6.53, 6.54, and 6.55 (reproduced in MPEP § *> 609.03<). Otherwise, applicant must follow the procedure set forth in 37 CFR 1.97 and 1.98 in order to ensure that the examiner considers the documents cited in the international search report.

Secondly, in the information disclosure statement filed August 22, 2005, applicant submits that copies of these references are contained on a CD-ROM. Notably, this submission is not in compliance with 37 CFR 1.52 which limits the submission of documents on compact disc to the Office to the following:

(i) A computer program listing (see § 1.96);

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[3] See Ragapathi et al (J. Immun., 174:5706-5712, 2005)

(ii) A "Sequence Listing" (submitted under § 1.821(c)); or

(iii) Any individual table (see § 1.58) if the table is more than 50 pages in length, or if the total number of pages of all of the tables in an application exceeds 100 pages in length, where a table page is a page printed on paper in conformance with paragraph (b) of this section and § 1.58(c).

Therefore, as legible copies of these citations were not properly submitted these citations fail to comply with 37 CFR 1.98(a)(2) and were not considered.

Applicant is invited to submit another Information Disclosure Statement following the procedure set forth in 37 CFR 1.97 and 1.98 for the Examiner to consider.

Claim Objections

10. (a) Claims 11 and 30 are objected to as being drawn in the alternative to the subject matter of a non-elected invention (i.e., the invention of Group XI).

(b) Claims 17 and 26 are objected to as being drawn in the alternative to the subject matter of a non-elected invention (i.e., the inventions of Group I-III and V-VII).

(c) Claim 1 is objected to for reciting "treatement". It appears that this is a typographical error and the claim should recite "treatment".

(d) Claims 3 and 32 are objected to for reciting "the tumor cell". In this case, claims 1 and 29 recite a plurality of tumor cells, so it appears the claims should recite "the tumor cells".

(e) Claim 4 is objected to for containing two commas following "carbohydrates".

(f) Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In this case,

Claim 28 recites administering the Lewis Y antibody during surgery, yet the preceding claim is already necessarily drawn to administering a Lewis Y antibody during surgery as the Lewis Y antibody is administered during an intraoperative treatment, i.e., during surgery.

(g) Claims 30 and 31 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In this case, these claims recite administering the Lewis Y antibody during the surgical intervention, yet the preceding claim is already necessarily drawn to administering a Lewis Y antibody during surgery as the Lewis Y antibody is administered during an intraoperative treatment; i.e., during surgery.

(h) Claim 17 is objected to for reciting "Lews Y". It appears that this is a typographical error and the claim should recite "Lewis Y".

(i) Claims 20-22 are objected to for reciting "does". It appears that this is a typographical error and the claim should recite "dose".

(j) Claim 26 is objected to for reciting "Glob H". It appears that this is a typographical error and the claim should recite "Globo H"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 6-9, 11, 13-15, 18-22, 34-36 and 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 6 and 33 are indefinite in the recitation of "according to an ADCC and CDC effector function". This recitation renders the claims indefinite because it cannot be determined how the immune system must be activated in "accordance to" an ADCC and CDC effector function. Must the antibody mediate ADCC and CDC? Is the cytotoxicity necessarily directed against the tumor cells? Notably, while antibodies are known to activate antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC), antibodies *per se* do not have "an ADCC and CDC effector function" as an antibody in and of itself does not cause ADCC and CDC. Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(b) Claims 7, 18, 19 and 34 are indefinite in the recitation of "an affinity corresponding to a dissociation constant" in claim 7. This recitation renders the claims indefinite because it cannot be determined to what extent the affinity of the antibody must *correspond to* the dissociation constant. How must the affinity correspond to the dissociation constant? Is it equal to the dissociation constant, similar to the dissociation constant, or does the affinity *correspond to* the dissociation constant in some other way? Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(c) Claims 9 and 36 are indefinite in the recitation of "wherein the antibody is used systemically" in claims 9 and 36. This recitation renders the claims indefinite because it cannot be determined how the antibody is systemically used. What does it

mean to use the antibody "systemically"? Is it administered systemically, or used systemically in some other way? How does one use an antibody "systemically"? Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(d) Claim 11 is indefinite in the recitation of "immediately during". This recitation renders the claims indefinite because it is unclear what immediacy of administering the antibody during surgery is necessary to administer an antibody immediately during the surgical intervention. How might one determine the immediacy necessary? When during the surgical intervention must the antibody be administered to fulfill the requirement of the immediacy? Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(e) Claims 8 and 35 are indefinite in the recitation of "derived from murine, chimeric, humanized, and/or human sources" in claims 8 and 35. This recitation renders the claims indefinite because it is unclear how or to what extent an antibody is necessarily "derived" from one or more of these sources? What is meant by a "humanized" source? Is the antibody a murine, chimeric, humanized, or human antibody? If so, how might an antibody be, e.g., both murine and human? Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(f) Claim 13 is indefinite in the recitation of "carried out for a determination regarding the malignancy of a tumor". This recitation renders the claim indefinite because it is unclear what determination about the tumor made? Is the tumor determined to be malignant or not? If so is the metastatic potential of the tumor

determined or is some other determination made about the malignancy of the tumor? Thus, it is submitted that the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(g) Claims 14-15 and 40 are indefinite in the recitation of "wherein the *antibody is determined on* the immunocomplex tumor tissue after the surgical intervention" in claim 14 and "wherein the *antibody is determined on* tumor cells in blood or serum samples" in claims 15 and 40. In this case, it cannot be ascertained what determination is necessarily made. Is the binding of the antibody, the amount of the antibody, the ability of the antibody to inhibit tumor cell dissemination, or is something else about the antibody determined on the tumor tissue or tumor cells? Accordingly, it is submitted that these claims fails to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

(h) Claims 20-22 are indefinite in the recitation of "said single [dose]". This limitation lacks antecedent basis, as claims 8 and 1 do not refer to any single dose. Therefore, it is unclear which if any single dose is being referred to. Accordingly, the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph

(i) Claims 41-43 are indefinite in the recitation of "said Kd value" in claims 41 and 42 and "said single dose" in claim 43. These limitations lack antecedent basis, as claims 40 and 29 do not refer to any Kd value or single dose. Therefore, it is unclear which if any Kd value or single dose is being referred to. Accordingly, the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth

under 35 U.S.C. § 112, second paragraph.

Accordingly, these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 22 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

Here, it has been presumed that claim 22 should properly depend from claim 9, as opposed to claim 8. Additionally, while it cannot be determined what single dose is being referred to in claim 43 due to its indefinite nature, claim 43 is included in this rejection as support for the language of the claim could not be found in the specification as filed.

Claim 22 is drawn to administering antibodies directed against a tumor-associated antigen in a single dose of at most 2 mg. Claim 43 recites a single dose of at most 2 mg.

In this case, claim 22 was added in the amendment filed August 22, 2005 and claim 43 was added in the amendment filed May 24, 2007. In these responses, Applicant has not indicated where support occurs in the specification for these newly added claims.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims". See M.P.E.P. § 714.02

and § 2163.06. Nevertheless, as M.P.E.P. § 2163 further states: "The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See *Wertheim*, 541 F.2d at 263, 191 USPQ at 97".

After reviewing the specification, it does not appear that the specification, including the claims, as originally filed, provide adequate support for these claims. Notably, page 15 of the specification, 3rd paragraph, discloses administering single doses of at least 50 mg, at least 100 mg or at least 200 mg of antibodies, but written support for the recitation in the claims of administering a single dose of at most 2 mg could not be found in the specification, as filed.

Therefore, it is submitted that the language of claims 22 and 43, which apparently fails to find adequate written support in the specification, including the claims, as originally filed, introduces new concepts and thereby violate the written description requirement of the first paragraph of 35 U.S.C 112.

This issue might be remedied if Applicant were to point to specific disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary support for the language of claims 22 and 43.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1-8, 10-15, 18-19 and 22 are rejected under 35 U.S.C. 102(b) as being

anticipated by US Patent No. 5,716,595 (Goldenberg et al, published 1998) as evidenced by Cellular and Molecular Immunology (Eds. Abass et al.; 1991; W.B. Saunders: Philadelphia; page 54).

Here, it has been presumed that claim 22 should properly depend from claim 9, as opposed to claim 8.

The claims are herein drawn to methods of administering antibodies to patients directed against a tumor associated antigen during surgery, wherein the antibody binds to the tumor cells during the surgery. The claims are further drawn to the antibody being directed against a protein surface antigen of an epithelial tumor cell (claims 3 and 4), administering an antibody mixture comprising antibodies having a specificity for tumor-associated antigens (Claim 5), the antibodies being derived from murine, chimeric, humanized or human sources (claim 8), the antibodies having a Kd value below 10^{-8} mol/l (claim 19), the antibodies being administered in a dose of at most 2 mg (claim 22) and the antibodies being administered locally (claim 10). Additionally, the claims are drawn to the surgery being carried out for biopsy and/or removal of the tumor or to determine the malignancy of the tumor (claims 12 and 13). Due to the indefinite nature of claims 6 and 14-15, the claims are interpreted to encompass administering antibodies to patients during surgery with any effect.

Goldenberg et al teach methods for the intraoperative treatment of epithelial derived tumors comprising locally administering antibodies to patients during surgery (see entire document, e.g., column 10, lines 31-61), wherein the antibodies are directed against epithelial tumor associated surface antigens or tumor associated antigens, such as antibodies directed against tumor associated surface antigen CEA and/or the tumor associated antigen CSAp (e.g., column 13, lines 8-18). Additionally, Goldenberg et al teach murine, human, humanized or chimeric antibodies (e.g., column 6, lines 51-57 and column 13, lines 1-7) and administering at most 2 mg of an antibody (column 15, lines 43-50). Finally, Goldenberg et al teach that surgeries are carried out to determine malignancy and/or to remove and/or treat the tumor (e.g., column 6, lines 25-35).

As evidenced by Cellular and Molecular Immunology, for antibodies specific for an antigen of interest, the binding constant (Kd) usually varies from about 10^{-7} M to 10^{-11}

M (page 54). Accordingly, although Goldenberg et al do not expressly teach using an antibody during surgery that binds, for example, the tumor associated surface antigen CEA and/or the tumor associated antigen CSAp, which has a binding constant below 10^{-8} mol/l, absent a showing of any difference, the antibodies used during surgery disclosed by the prior art are deemed the same as the claimed antibodies used during surgery.

Additionally, while Goldenberg et al do not expressly teach that the antibodies bind to the tumor cells during surgery, the processes of Goldenberg et al are manipulatively and materially indistinguishable from the claimed processes. Thus, absent a showing of any difference, the claimed processes are deemed the same as that disclosed in the prior art.

Therefore, Goldenberg et al anticipate these claims.

17. Claims 1-8, 10-15 and 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 6,107,102 (Ferrari et al, published 2000) as evidenced by Cellular and Molecular Immunology (Eds. Abass et al.; 1991; W.B. Saunders: Philadelphia; page 54).

The claims are herein drawn to methods of administering antibodies to patients directed against a tumor associated antigen during surgery, wherein the antibody binds to the tumor cells during the surgery. The claims are further drawn to the antibody being directed against a protein surface antigen of an epithelial tumor cell (claims 3 and 4), administering an antibody mixture comprising antibodies having a specificity for tumor-associated antigens (Claim 5), the antibodies being derived from murine, or human sources (claim 8), the antibodies being administered locally (claim 10) and the antibodies having a Kd value below 10^{-8} mol/l (claim 19). Additionally, the claims are drawn to the surgery being carried out for biopsy and/or removal of the tumor or to determine the malignancy of the tumor (claims 12 and 13). Due to the indefinite nature of claims 6 and 14-15, the claims are interpreted to encompass administering antibodies to patients during surgery with any effect.

Ferrari et al teach methods for the intraoperative treatment of epithelial derived

tumors 'comprising locally administering antibodies to patients during tumor removal surgery (see entire document, e.g., column 10, lines 31-61), wherein the antibodies are directed against epithelial tumor associated surface antigens or tumor associated antigens, such as antibodies directed against the tumor associated surface antigen TAG-72 and/or the tumor associated antigen collagen IV and wherein the antibodies bind to the tumor cells during surgery (see entire document, e.g., column 19, line 57 to column 20, line 15) and column 11, lines 34-46). Additionally, Ferrari et al teach murine or human antibodies (e.g., column 11, lines 34-46 and column 16, lines 9-13).

As evidenced by Cellular and Molecular Immunology, for antibodies specific for an antigen of interest, the binding constant (Kd) usually varies from about 10^{-7} M to 10^{-11} M (page 54). Accordingly, although Ferrari et al do not expressly teach using an antibody during surgery that binds, for example, the tumor associated surface antigen TAG-72 and/or the tumor associated antigen collagen IV protein, which has a binding constant below 10^{-8} mol/l, absent a showing of any difference, the antibodies used during surgery disclosed by the prior art are deemed the same as the claimed antibodies used during surgery.

Additionally, while Ferrari et al do not expressly teach that the surgery was carried out for the purpose of making a determination regarding the malignancy of the tumor, the process of Ferrari et al is materially and manipulatively indistinguishable from the claimed process and therefore, absent a showing of any difference, the process disclosed by the prior art is deemed the same as the claimed process.

Therefore, Ferrari et al anticipate these claims.

18. Claims 1-15 and 18-22 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,949,342 (Golub et al, published September 2005).

Here, it has been presumed that claims 20-22 should properly depend from claim 9, as opposed to claim 8.

The claims are herein drawn to methods of administering antibodies to patients directed against a tumor associated antigen during surgery, wherein the antibody binds

to the tumor cells during the surgery. The claims are further drawn to the antibody being directed against a protein surface antigen of an epithelial tumor cell (claims 3 and 4), administering an antibody mixture comprising antibodies having a specificity for tumor-associated antigens (Claim 5), the antibodies being derived from murine, chimeric, humanized or human sources (claim 8), the antibodies being administered in a dose of at least 200 mg (claim 21) or at most 2 mg (claim 22), the antibodies having a Kd value below 10^{-8} mol/l (claim 19) and the antibodies being administered systemically (claim 9) or locally (claim 10). Additionally, the claims are drawn to the surgery being carried out for biopsy and/or removal of the tumor or to determine the malignancy of the tumor (claims 12 and 13). Due to the indefinite nature of claims 6 and 14-15, the claims are interpreted to encompass administering antibodies to patients during surgery with any effect.

Golub et al teach methods of treating prostate tumors comprising administering antibodies to patients during surgery either intravenously (i.e. systematically) and/or locally (see entire document, e.g., column 30, lines 1-49), wherein the antibodies are directed against a tumor associated surface antigens or tumor associated antigens, such as antibodies directed against Platelet Derived Growth Factor Receptor, a prostatic epithelial tumor cell associated surface antigen and/or antibodies directed against HoxC6, a prostatic epithelial tumor cell associated antigen (e.g., column 10, lines 36-67). Additionally, Golub et al teach murine, human, humanized or chimeric antibodies (e.g., column 19, lines 53-65), antibodies having a Kd value below 10^{-8} mol/l, (e.g., column 21, lines 6-13) and administering antibodies in a dose of at least 200 mg or at most 2 mg (column 29, lines 36-50). Finally, Golub et al teach that surgeries are carried out to obtain biopsies to determine malignancy and/or remove the tumor (e.g., column 1, lines 34-55 and column 9, lines 32-58).

While, Golub do not expressly teach that the antibodies bind to the tumor cells during surgery, the processes of Goldenberg et al are manipulatively and materially indistinguishable from the claimed processes. Thus, absent a showing of any difference, the claimed processes are deemed the same as that disclosed in the prior art.

Therefore, Golub et al anticipate these claims.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 1, 9, 17, 20, 25-33, and 35-40 are rejected under 35 U.S.C. 103(a) as

being unpatentable over US Patent No. 5,716,595 (Goldenberg et al, published 1998), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000).

The claims are herein drawn to methods of administering Lewis Y antibodies to patients during surgery, wherein the antibody binds to the tumor cells during the surgery. The claims are further drawn to the antibody being administered systematically in a dose of at least 100 mg, administered in a single dose of at most 2 mg or administered locally, the antibodies being derived from murine, chimeric, humanized or human sources. Additionally, the claims are drawn to the surgery being carried out for biopsy and/or removal of the tumor or to determine the malignancy of the tumor. Due to the indefinite nature of claims 33 and 40, the claims are interpreted to encompass administering Lewis Y antibodies to patients during surgery with any effect.

Goldenberg et al teach what is set forth in the above 102 (b) rejection.

However, Goldenberg et al do not expressly teach administering Lewis Y antibodies to patients or administering at least 100 mg of an antibody to a patient.

These deficiencies are made up for in the teachings of Schlimok et al and Crisan et al. Schlimok et al teach that disseminated breast epithelial tumor cells express a surface antigen named Lewis Y and that administering Lewis Y antibodies to breast cancer patients systemically in doses of 100 mg inhibits tumor cell dissemination in patients with large numbers of disseminated tumor cells present in their bone marrow (see entire document, e.g., abstract, page 1802, Tables 3 and 4). Crisan et al teach that breast tumor epithelial cells can be mobilized to disseminate from the tumor site during breast surgery as patients monitored for disseminated tumor cells before and after breast surgery show increased levels of circulating disseminated cells after surgery (see entire document, e.g. abstract and page 36, left column).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to systematically administer Lewis Y antibodies to patients during surgery in doses of 100 mg or according to the methods taught by Goldenberg et al, as Schlimok et al teach that the Lewis Y antibody inhibits breast cancer dissemination and Crisan et al teach that surgery increases breast

epithelial cell dissemination.

One of ordinary skill in the art would have been motivated at the time the invention was made to do so, and would have had a reasonable expectation of success, because Crisan et al teach that surgery increases the number of disseminated cells and Schlimok et al teach that Lewis Y antibodies can be systemically administered to breast cancer patients and that these antibodies inhibit tumor cell dissemination in patients with increased numbers of circulating cells.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to locally administer the Lewis Y antibody to the tumor site as Goldenberg et al teach methods of treating tumors by locally applying antibodies directed to tumor antigens and Crisan et al teach that tumor cells are mobilized to disseminate during surgery.

One of ordinary skill in the art would have been motivated at the time the invention was made to do so, and would have had a reasonable expectation of success, because Crisan et al teach that tumor cells are mobilized during surgery and therefore one of skill in the art would have motivated to administer the Lewis Y antibody locally according to the methods of Goldenberg to prevent this mobilization.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

22. Claims 21 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,716,595 (Goldenberg et al, published 1998), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) as applied to claims 1, 9, 17, 20, 25-33 and 35-36 and 38-40 above, and further in view of US Patent 5,792,456 (Yelton et al, published 1998).

Claims 21 and 34 are further drawn to the Lewis Y antibodies having a Kd value below 10^{-8} mol/l or the Lewis Y antibody being administered at a dose of at least 200 mg.

Goldenberg et al, Schlimok et al and Crisan et al teach this which is set forth above.

However, neither Goldenberg et al, Schlimok et al and Crisan et al explicitly teach administering to patients Lewis Y antibodies having a Kd value below 10^{-8} mol/l or the Lewis Y antibody being administered at a dose of at least 200 mg.

Yelton et al teach methods of administering Lewis Y antibodies to patients and Lewis Y antibodies with a Kd value below 10^{-8} mol/l (see entire document, column 33, line 61 to column 36, line45) and the Lewis Y antibody being administered at a dose of at least 200 mg (e.g column 20, line 39 to column 22, line 47).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to furthermore treat patients during surgery with Lewis Y antibodies with Kd values below 10^{-8} mol/l and to administer the Lewis Y antibody at a dose of at least 200 mg.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to do so because Lewis Y antibodies with a Kd values below 10^{-8} mol/l would have higher affinity for the disseminated tumor cells and higher doses of antibody would target more disseminated tumor cells. Thus, as Schlimok et al teach that Lewis Y antibodies inhibit tumor cell dissemination, one of skill in the art would have been motivated to use the higher affinity antibodies and dosing schedules of Yelton et al and as these higher affinity antibodies and dosing schedules were known in the art and one of skill in the art would have had a reasonable expectation of success in practicing the claimed methods.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

23. Claims 1, 9, 17, 20, 25-33 and 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over by US Patent 6,107,102 (Ferrari et al, published 2000), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000).

The claims are herein drawn to methods of administering Lewis Y antibodies to patients during surgery, wherein the antibody binds to the tumor cells during the surgery. The claims are further drawn to the antibody being administered systematically

in a dose of at least 100 mg, or administered locally, the antibodies being derived from murine, chimeric, humanized or human sources. Due to the indefinite nature of claims 33 and 40, the claims are interpreted to encompass administering Lewis Y antibodies to patients during surgery with any effect.

Ferrari et al teach what is set forth in the above 102 (b) rejection.

However, Ferrari et al not expressly teach administering Lewis Y antibodies to patients or administering at least 100 mg of an antibody to a patient.

These deficiencies are made up for in the teachings of Schlimok et al and Crisan et al. Schlimok et al teach that disseminated breast epithelial tumor cells express a surface antigen named Lewis Y and that administering Lewis Y antibodies to breast cancer patients systemically in doses of 100 mg inhibits tumor cell dissemination in patients with large numbers of disseminated tumor cells present in their bone marrow (see entire document, e.g., abstract, page 1802, Tables 3 and 4). Crisan et al teach that breast tumor epithelial cells can be mobilized to disseminate from the tumor site during breast surgery as patients monitored for disseminated tumor cells before and after breast surgery to obtain biopsies for a determination regarding the malignancy of the tumor show increased levels of circulating cells after surgery (see entire document, e.g. abstract and page 36, left column).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to systematically administer Lewis Y antibodies to patients during breast cancer surgery in doses of 100 mg or by the methods of Ferrari, as Schlimok et al teach that the Lewis Y antibody inhibits breast cancer dissemination and Crisan et al teach that surgery increases breast epithelial cell dissemination.

One of ordinary skill in the art would have been motivated at the time the invention was made to do so, and would have had a reasonable expectation of success, because Crisan et al teach that surgery to determine the malignancy of a tumor increases the number of disseminated cells and Schlimok et al teach that Lewis Y antibodies can be systemically administered to breast cancer patients and that these antibodies inhibit tumor cell dissemination in patients with increased numbers of

circulating cells.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to locally administer the Lewis Y antibody to the tumor site as Ferrari teach methods of treating tumors by locally applying antibodies directed to tumor antigens during surgery and Crisan et al teach that tumor cells are mobilized to disseminate during surgery.

One of ordinary skill in the art would have been motivated at the time the invention was made to do so, and would have had a reasonable expectation of success, because Crisan et al teach that tumor cells are mobilized during surgery and therefore one of skill in the art would have motivated to administer the Lewis Y antibody locally according to the methods of Ferrari to prevent this mobilization.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

24. Claims 21 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,107,102 (Ferrari et al, published 2000), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) as applied to claims 1, 9, 13, 17, 20, 25-33 and 35-40 above, and further in view of US Patent No. 5,792,456 (Yelton et al, published 1998).

Claims 21 and 34 are further drawn to the Lewis Y antibodies having a Kd value below 10^{-6} mol/l or the Lewis Y antibody being administered at a dose of at least 200 mg.

Ferrari et al, Schlimok et al and Crisan et al teach this which is set forth above.

However, neither Ferrari et al, Schlimok et al and Crisan et al explicitly teach administering to patients Lewis Y antibodies having a Kd value below 10^{-6} mol/l or the Lewis Y antibody being administered at a dose of at least 200 mg.

Yelton et al teach methods of administering Lewis Y antibodies to patients and Lewis Y antibodies with a Kd value below 10^{-6} mol/l (see entire document, column 33, line 61 to column 36, line45) and the Lewis Y antibody being administered at a dose of at least 200 mg (e.g column 20, line 39 to column 22, line 47).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to furthermore treat patients during surgery with Lewis Y antibodies with Kd values below 10^{-6} mol/l and to administer the Lewis Y antibody at a dose of at least 200 mg.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to do so because Lewis Y antibodies with a Kd values below 10^{-6} mol/l would have higher affinity for the disseminated tumor cells and higher doses of antibody would target more disseminated tumor cells. Thus, as Schlimok et al teach that Lewis Y antibodies inhibit tumor cell dissemination, one of skill in the art would have been motivated to use the higher affinity antibodies and dosing schedules of Yelton et al and as these higher affinity antibodies and dosing schedules were known in the art and one of skill in the art would have had a reasonable expectation of success in practicing the claimed methods.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

25. Claims 1, 17, and 25-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,949,342 (Golub et al, published September 2005), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000).

The claims are herein drawn to methods of administering Lewis Y antibodies to patients during surgery, wherein the antibody binds to the tumor cells during the surgery. The claims are further drawn to the antibody being administered systematically in a dose of at least 200 mg, administered in a single dose of at most 2 mg or administered locally, the antibodies being derived from murine, chimeric, humanized or human sources and the Lewis Y antibody having a Kd value below 10^{-6} mol/l. Additionally, the claims are drawn to the surgery being carried out for biopsy and/or removal of the tumor or to determine the malignancy of the tumor. Due to the indefinite nature of claims 33 and 40, the claims are interpreted to encompass administering Lewis Y antibodies to patients with any effect.

Golub et al teach what is set forth in the above 102 (b) rejection.

However, Golub et al not expressly teach administering Lewis Y antibodies to patients.

These deficiencies are made up for in the teachings of Schlimok et al and Crisan et al. Schlimok et al teach that disseminated breast epithelial tumor cells express a surface antigen named Lewis Y and that administering Lewis Y antibodies to breast cancer patients systemically inhibits tumor cell dissemination in patients with large numbers of disseminated tumor cells present in their bone marrow (see entire document, e.g., abstract, page 1802, Tables 3 and 4). Crisan et al teach that breast tumor epithelial cells can be mobilized to disseminate from the tumor site during breast surgery as patients monitored for disseminated tumor cells before and after breast surgery show increased levels of circulating cells after surgery (see entire document, e.g. abstract and page 36, left column).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to systematically administer Lewis Y antibodies to patients during breast cancer surgery using the methods of administering antibodies during surgery taught by Golub et al, as Schlimok et al teach that the Lewis Y antibody inhibits breast cancer dissemination and Crisan et al teach that surgery increases breast epithelial cell dissemination.

One of ordinary skill in the art would have been motivated at the time the invention was made to do so, and would have had a reasonable expectation of success, because Crisan et al teach that surgery increases the number of disseminated cells and Schlimok et al teach that Lewis Y antibodies can be administered to breast cancer patients to inhibit tumor cell dissemination in patients with increased numbers of circulating tumor cells.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 1-8, 11-15 18-19 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 9-10, 14, 16-20 and 24-27 of copending Application No. 10/558,166 as evidenced by Cellular and Molecular Immunology (Eds. Abass et al.; 1991; W.B. Saunders: Philadelphia; page 54). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5, 9-10, 14, 16-20 and 24-27 of copending Application No. 10/558,166 are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Here, it has been presumed that claim 22 should properly depend from claim 9,

as opposed to claim 8.

The instant claims are described supra.

Claims 1-5, 9-10, 14, 16-20 and 24-27 of copending Application No. 10/558,166 are drawn to methods administering antibodies to patients during surgery (see claim 27 in particular), wherein the antibody is specific to an epithelial tumor surface antigen or wherein the antibody is administered locally or systemically in a dosage of 0.1 to 1 mg.

As evidenced by Cellular and Molecular Immunology, for antibodies specific for an antigen of interest, the binding constant (Kd) usually varies from about 10^{-7} M to 10^{-11} M (page 54). Accordingly, although claims 1-5, 9-10, 14, 16-20 and 24-27 of copending Application No. 10/558,166 do not expressly teach using an antibody during surgery which has a binding constant below 10^{-8} mol/l, absent a showing of any difference, the antibodies used during surgery disclosed by claims 1-5, 9-10, 14, 16-20 and 24-27 of copending Application No. 10/558,166 are deemed anticipate the claimed subject matter of the instant application

Accordingly, the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

28. Claims 1-8, 11-15 18-19 and 22 are directed to an invention not patentably distinct from claims 1-5, 9-10, 14, 16-20 and 24-27 of commonly assigned application 10/558,166. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the above provisional rejection of the claims on the ground of nonstatutory obviousness-type double patenting.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending application 10/558,166, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if

the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

29. No claims are allowed.

30. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bigner et al (US Patent 5,624,659, 1997) teach locally administering an antibody directed against the tumor associated antigen, tenascin into surgical resection cavities of glioblastoma patients during surgery.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

bd
August 2, 2007